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CONTENTS:

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THE WAR WITH THE MICROBES.*

FROM the moment that man made his appearance in the world there has been perpetual warfare between himself and everything animate and inanimate upon the earth. To a great extent this has been an aggressive strife, man's every effort being exerted to compel nature to contribute to his comfort, welfare and advancement by the subjugation of her materials and forces. It was many centuries, however, before he recognized that there were certain unknown insidious enemies, which often rendered fruitless his simple household occupations, defied his every effort at control and sometimes menaced even his well-being and life. Though in 1675 Leeuwenhoeck discovered, with a powerful magnifying glass, certain minute organisms in decomposing animal matter, it was not until nearly two centuries later that their true significance was recognized, and Davaine first demonstrated the positive connection between these minute forms of life and disease. When animal and vegetable life ceased, in accordance with the laws of nature, they were supposed to be changed by purely chemical actions, so that their elements were again returned to the earth and air to supply food for other plants and animals. This destruction was considered to be wrought simply by the oxygen of the air, and the process of

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fermentation was thought to be due to a similar cause. It had been known for ages that the juice of the grape, if allowed to stand, underwent changes by which its character was modified and wine was formed, or this change might be allowed to progress further until the juice had been converted into vinegar and finally carbon dioxide gas and water. These alterations, those which take place in the digestive tract of animals and are involved in the conversion of dead animal and plant matter into their simplest constituents, were classed under the general head of fermentations.

The fermentations, especially that of wine, an Italian chemist, Fabroni, in 1822, supposed to be induced by a substance of vegetable origin, but closely allied to the white of egg. He considered this material identical with the gluten of cereals and gave to it the name of the 'principle vegeto-animal.' For nearly forty years afterwards this theory was applied by chemists to all fermentations. It was supposed that the albuminoid substance present exposed to the oxygen of the air experienced a progressively variable alteration, that diverse modifications of matter were produced which constituted the ferments of diverse nature. The fermentation was the result of the molecular movement thus communicated. These theories were based upon an erroneous interpretation of what occurred under certain conditions. There exists in wine, when it is being converted into vinegar, a substance which acts to bring about this modification, but this is not dead albuminoid matter, but a living plant. This fact the lamented chemist, Pasteur, demonstrated in his careful studies upon the production of wine and its conversion into vinegar. Before this time, it is true, there were many who failed to accept the theory of spontaneous oxidation, and endeavored to show that if fermentable liquids were boiled in flasks which were then immediately sealed, the fermentation could not take place. But this did not fulfill the demands of one school of chemists, viz., that plenty of oxygen gas should always be present. When the liquid was boiled in contact with air which had previously been drawn through sulphuric acid, it was claimed that the air had undergone some chemical change, so it was not until 1854 that this objection was overcome by previously passing the air in the presence of which boiling took place through cotton, and it was then that this school of chemists found their theories in danger. Pasteur demonstrated that the plant present in the preparation of vinegar was the simplest form of life, a cell which could be easily destroyed by heat. Its presence was absolutely necessary for fermentation, and without the living cell no amount of dead vegetable matter could cause the peculiar molecular disarrangement which had been claimed. While Liebig had contended that as long as the juice of the grape remained away from contact with the oxygen of the air the necessary motion could not be imparted to the molecules, which movement subsequently caused the phenomena of fermentation. Thus was brought to an end the strife between the two schools of vitalists and chemists; the one school of chemists demanding the presence of ogygen only, the other the presence of a living plant cell in addition to oxygen. From this strife of the two schools was evolved in reality a new science and new theories, which have made the past thirty years marvelous in their explanations of many of the simplest phenomena of plant and animal life and death, placed the practice of medicine upon a scientific basis and rendered possible an intelligent system of agriculture and animal husbandry.

Pasteur's discoveries also served to explain the true cause of the poisonous properties of spoiled meats and other foods, stagnant

water, and water from marshy countries. For more than half a century before this time a number of investigators had proved the dangerous character of old sausage meats, bread and the like. Kerner concluded that they contained a fatty acid to which the poisonous action was due; others confirmed these ideas and came to similar conclusions in regard to poisonous cheese. In 1856 Panum asserted, as a result of his studies upon the poisons found in putrid animal matter, that these poisons might be formed by some active plant cell, but their injurious effect was independent of these cells. He demonstrated that fixed non-volatile poisons could be extracted from putrid matter which were soluble in water and alcohol, not destroyed by heat, and produced the same effects after they had been submitted to a high temperature as before. These poisons he found to be intense in their action, 0.012 grams sufficing to cause the death of a small animal. In 1866 Bence-Jones obtained from the liver a substance which, with dilute sulphuric acid, gave a bright blue fluorescence like that noted in similar solutions of quinine. Probably this was the product of what we now call fluorescing bacteria.

The work of Pasteur threw light upon the origins of these poisons. As the ferment causes the alteration in the grape juice, so do microscopic forms of life bring about the changes which take place in dead animal and vegetable matter, and also those conditions in the living body which we call disease.

Many of these microscopic forms of single-celled plants, *the bacteria*, have their natural habitat upon dead organic matter, but they may flourish in the living body and are almost unlimited in variety, appearance and behavior. It is possible also to cultivate them upon specially prepared solutions after their individual peculiarities have been studied. Some thrive best in light, others in darkness; some like a goodly supply of oxygen, others prefer nitrogen; some are very sensitive to changes of temperature, while others readily accustom themselves to vicissitudes.

These different bacteria further are somewhat eccentric within as well as without the animal body. Some, as the diphtheria germs, find their most comfortable habitat upon certain mucous membranes, others in the lungs, some in the digestive tract, still others in the blood, while others again confine themselves to certain external cells and membranes. In their artificial cultivation this eccentricity is equally apparent. While nearly all thrive upon a beef broth, some prefer the beef broth with an excess of acid, others with an excess of alkali. Some demand the addition of sugar or glycerine, others the addition of sugar together with acid, while some are satisfied with a diet of phosphates, salt and water. These peculiarities have to be studied for each germ, and while many can accommodate themselves to their surroundings, and while the same germ grown upon different media produces the *same substances*, the amount of each substance is a varying one, and in cultivating them artificially we must find which diet gives rise to the largest amount of the most active products.

Shortly after the work of Panum just referred to, the Italian chemist Selmi outlined methods of extracting poisonous principles from dead animal matter, and gave to these substances the name ptomaines, on account of their origin. Later, in 1876, the first analysis of a ptomaine was made by Nencki and its formula determined. Further experiments showed that volatile and non-volatile substances, alkaline in character, could be obtained from various portions of the animal body, often from fresh material and also from the cultures of bacteria. These ptomaines were found to resemble the alkaloids in their chemical reactions.

In 1882–83 Brieger succeeded in separa-

ting and determining a number of these ptomaines, from the brain, from fish muscarin, from decomposed glue, neuridine and dimethyl amine, muscarin, etc. From pure cultures of the typhoid germ he obtained a substance, typhotoxin, which produced typhoid symptoms, and from cultures of the tetanus germ tetanin, which caused convulsions. The presence of similar poisonous bases was demonstrated in cultures of the cholera, hog cholera, anthrax, pyogenes aureus and like active bodies were isolated from cheese, milk, ice cream, sausage and other foods which had caused sickness.

The isolation of these poisons from bacterial cultures gave rise to the belief that they were the bodies which caused the fatal effects of disease. But while in many instances they produced the characteristic symptoms, in others they were not sufficient to account for all the phenomena. For example, from cultures of the tetanus germ it was possible to isolate a base that had but slight poisonous properties, while the culture liquid from which this was obtained after all the germs had been removed was ten thousand times more poisonous than the base secured. Non-poisonous ptomaines were also obtained from cultures of disease-producing bacteria, and, in fact, the majority of ptomaines were found to be non-poisonous.

The next question was, if in the culture liquids freed from bacteria, poisonous substances are obtained, and if they do not belong to the class of ptomaines, how shall they be identified and classified? In 1886 Mitchell and Reichert, while studying the venoms of serpents, noted that these poisons belonged to a class of bodies different from the ptomaines, viz., to the group called proteids. Shortly after, Roux and Yersin, in their studies upon the diphtheria poison, demonstrated that this was a substance which resembled the ferments and led them to think that an enzyme, as it is called, a substance like pepsin, was the active poison, and that this enzyme was in some way elaborated by the germ. Other investigators had found a similar substance in tetanus and hog cholera cultures, and a reinvestigation by Brieger of a number of bacterial cultures showed that by precipitation with ammonium sulphate and alcohol very poisonous substances giving proteid reactions could be obtained. Proteids of various characters belonging to different classes were obtained from cultures of many bacteria. About this time it was shown that certain plants of a higher order contained poisonous bodies of a like proteid character. An albumose abrin was obtained from the Jequirity seeds and ricin from the castor-oil bean. These were intensely poisonous, $\frac{1}{1000000}$ of a grain of abrin being sufficient to kill an animal weighing one kilogram, or the $\frac{1}{100}$ of a grain should be a fatal dose for a man weighing about 130 pounds.

A relationship was thus established between the poisons from higher plants and from the lowest plants and certain animals. Was this poisonous property of these bacterial substances due to a true proteid, or was there an admixture of an active ferment-like substance with the proteid, and are these poisons mechanically carried down in the process of precipitation of the albuminoid matter in the culture liquids? Experiments show that while the poisons may be proteids, it is more than probable that they are simply carried down with proteid matter as indicated. Brieger in 1893, in view of the results so far obtained, endeavored to isolate the pure poison from cultures of the tetanus bacillus. The cultures were first filtered through porous porcelain, a Chamberland or Monroe filter tube, for instance, and the liquid which passed through was treated with a concentrated solution of ammonium sulphate. This preciptated the poisons and a number of other substances

which gave proteid reactions. After purification and dialysis the poison was obtained as yellow soluble flakes which no longer gave proteid reactions. It was a substance in which there was no noticeable phosphorus nor sulphur. It was thus proved that the tetanus poison belonged neither to the ptomaines before referred to, nor to the proteids. The poison, while not perfectly pure, was purer than any ever before obtained, and was so poisonous that a mouse weighing $\frac{1}{2}$ oz. was killed by $\frac{1}{1,128,000}$ part of a grain, while $\frac{1}{280}$ of a grain should kill a man weighing 150 lbs.

It is not difficult to understand how if the tetanus bacillus outside of the body can produce such powerful poisons, it can give rise in the animal organism to serious troubles. The diphtheria bacillus is another germ which forms very powerful poisons in the solutions upon which it feeds. As already mentioned, some authors, Roux and Yersin, believe that this poison also belongs to the ferments like trypsin and pepsin, while Brieger and Fraenkel thought it was a toxalbumin. We find after the germ has been removed from the culture liquid by filtration, that the poison can be separated by calcium phosphate or ammonium sulphate, just like the tetanus poison. In the purest condition in which it has been so far obtained it fails to give the proteid reaction, and $\frac{1}{64}$ of a grain will kill a guinea pig. It dialyses readily. Bodies of a similar kind have been obtained from cholera, glanders, swine plague, tuberculosis, and anthrax cultures, while many other bacteria produce soluble intensely poisonous substances in artificial cultures as well as inside the animal body.

These products are all characteristic of the individual organism. The conditions under which the most poisonous ones are formed seem to be dependent partly, we may say, upon the humor of the germ and also upon the food offered for its use. It appears, for example, in connection with the diphtheria germ that, if there happens to be present in the beef broth upon which it is being cultivated, an undue amount of glucose and an insufficient supply of alkali, that, instead of producing a very active poison, the substance secreted is much less harmful. This is accounted for by the supposition that the glucose is decomposed into acid which, in its turn, neutralizes or decomposes the poison ordinarily produced by the germ. These poisons, it was originally supposed, resulted from the decomposition of the food of the germ, just as soluble and assimilable albuminoids are produced by the acids and ferments of the animal body from the insoluble albuminoids that are ingested as food. It has been found, however, that in most instances the poison of the germ is in solution in quantity only after the germs themselves have become partially disintegrated. In other words, the active bacterial poisons seem to be products of the cell and retained within the cell until the latter dies and the cell membrane is broken, permitting the passage into the surrounding liquid of the poison. What then is the true nature of these poisons if they belong neither to the bases nor to the proteids or toxalbumins? That, unfortunately, is one of the problems to which, up to the present time, chemical research has not been able to give a definite answer; and this, because, as we have already noted, the poisons of these bacteria are so tremendously active and consequently produced in proportionately small amount, even when a large quantity of the culture media is used, that it has so far been a matter almost of impossibility to separate a sufficient quantity of these poisonous principles to purify them perfectly for chemical analysis. Perhaps this object has been attained more nearly than ever before by some workers in the Biochemic Laboratory in this city, who have succeeded in

separating from cultures of the tuberculosis germ a crystalline poison with constant melting point and a constant composition. This is not the only poison produced by the tuberculosis germ, but that it is one of the principles which is responsible for much of the trouble with this disease is beyond doubt. These special poisonous principles, which are so difficult to obtain pure, we designate by the name toxines, to distinguish them from the ptomaines and proteid substances before mentioned. Another difficulty which is always encountered in extracting the poisons of bacteria is their instability. The material with which an experiment is begun may be very poisonous, but the processes of precipitation and extraction through which it must be passed in order to obtain a desired substance are such that often, long before the final stages have been reached, the nature of the poisons has undergone an entire change due to the chemical processes which have necessarily been applied.

We have said that the poisons of the germ were synthetic products which were built up within the cell wall. Some of these easily pass through the cell wall, due probably to the greater permeability of the living membrane; others are retained within the cell wall only to pass into solution when these walls are broken down. Tetanus, diphtheria and swine plague allow this diffusion to take place very rapidly, while with other germs, like typhoid fever, anthrax, cholera, glanders, tuberculosis, the poison is produced and retained within the cell more firmly during the life of the latter. As the germs die, however, in artificial cultures, the cell walls gradually disintegrate and the poison passes out into the surrounding liquid. In the case of tuberculosis and glanders a strong solution of these cell poisons in the surrounding liquid upon which the germ has been feeding gives tuberculin and mallein, the two diagnostic agents which have been of inestimable value in detecting latent disease in men and animals and thus preventing the spread of untold evils.

Thus the warfare first began by the chemist with the microbes in identifying their character and relation to disease has been prosecuted for little more than a decade in endeavoring to detect the true character of the insidious poisons with which their arrows are tipped. To a certain extent, as we have seen, this warfare has been a successful one in so far that the poisons have been hunted and driven to their last stronghold, which, ere long, with the many workers in attack, must yield as heretofore to superior forces. But while this search for the pure poisons has been in progress the chemist has not been idle in endeavoring to counteract these poisons, the nature of which he did not thoroughly understand, but the evil effects of which were only too apparent. While Jenner in vaccination for small-pox, and Pasteur with his method of vaccination for anthrax, had shown that it was possible to protect animals and men from a virulent attack of disease by giving them first a mild attack, (though, by the way, there are a few who contend even to-day that vaccination is useless), it remained for Salmon, his assistant, and Smith in this city to demonstrate, in 1882, that the poisons of germs could be used by men and animals to fortify themselves against the attacks of these same bacteria. This could be accomplished by introducing into the circulation of the animal a small quantity of the poison of the germ, so that when the germ itself was injected the poison which it produced was without effect. What had been found true for one disease of animals proved also to be true for many others, and chemical vaccination was tried for diphtheria, tetanus, anthrax, cholera, typhoid fever, tuberculosis, glanders and a number of other diseases.

But this discovery led to another, important and far-reaching. Fodor showed that the blood serum of animals, made immune to a particular disease by injecting the animal with the poison which this germ formed, had the effect of destroying the germ of the disease. This excited renewed interest in the study of the blood, and within a few years it was demonstrated by the work of many, some in this city in the laboratories before mentioned, that this serum from previously immunized animals, not only had the property of conferring immunity upon other animals, but also of checking the disease after it had once begun. How thoroughly this fact was demonstrated, first by Behring and subsequently by Roux and others in connection with diphtheria and tetanus, has been dwelt upon often, and we know of the many thousands of lives that have been saved by the use of antitoxic serums.

To prepare these the solution of the toxins, which we have before described, are injected into different animals, preferably horses, and at the end of six to twelve weeks the blood of these animals is found to yield a serum containing substances possessing both immunizing and curative properties which we call antitoxines. The active principle of this serum is present in a comparatively small quantity, but its influence is enormous. It does not appear to be a substance which directly chemically neutralizes the poison, but counteracts its effects within the animal in some unknown way.

But some of our friends may ask: Were not these facts discovered first by the use of animals, and hence has not this knowledge, though of inestimable value to mankind, been too dearly bought? Yes, perhaps, a score or two of guinea pigs and sweet, lovely rats and mice have sacrificed their lives for humanity's sake. But this knowledge could not have been gained in any other way unless by the sacrifice of human life. What mother would hesitate to sacrifice a thousand guinea pigs for the life of her child, or, on the other hand, would wish her child to serve as the subject of experiment for others?

I have often been asked if the horses placed under this treatment for the production of antitoxines suffer. I think not and, as an illustration, will relate an incident which has come under my own observation, in the study of the antitoxins of the dread disease, tuberculosis. A well-blooded horse, gentle in every particular, except that he would run away upon the slightest provocation, seemed to be a suitable subject for some work. Accordingly he received an injection of the poison of the tuberculosis germ with the expectation that so high strung an animal would rebel against these pleasant familiarities. But he was entirely too wise for this. He submitted quietly and seemed much interested while by means of a hypodermic syringe a small quantity of the poison was ejected beneath his skin. A few days afterwards when the operation was repeated it would have been reasonable to expect that if there had been any discomfort the horse would have rebelled against the procedure. Did this happen? Not by any means. As soon as he observed the doctor appear with the syringe and bottle he trotted toward him with pleasure, stood quietly looking around with intelligence, while the injection was made and ever afterwards lent himself to the experiment with as much evident pleasure and interest as that of the investigators, apparently thoroughly appreciating its object.

It would hardly be fair to say that this dumb animal was endowed with more intelligence than some of our ill-informed but well-meaning friends, and yet would its actions not seem to indicate a high regard for scientific work and disclaimer of suffering?

Is it that they are instigated by a desire to inflict torture that scores of investigators

have sacrificed their lives in searching for the poisons of dangerous bacteria and their antitoxins? Is it inhumanity which spurs them on at imminent personal risk in their efforts, which are daily yielding new and brilliant results to find means for controlling a disease which annually causes one-seventh of the deaths of the population of the globe?

However, it is not only for protection against the two diseases, tetanus and diphtheria, just mentioned, that antitoxic serums can be prepared. Recent investigations have proved that typhoid fever, cholera, anthrax, the plague, etc., are amenable to similar treatment and in the same department in this city that chemical vaccination received its first impetus, but by workers in the Biochemic laboratory it has been demonstrated that two diseases that cause such losses to the farmers of the country may be controlled by antitoxic serums. Investigators in this same laboratory have shown also that a substance antitoxic to tuberculosis can be produced in the serum of animals when they are properly treated, which has undoubted and pronounced effect in checking experimental tuberculosis in small animals. When we inquire the character of these antitoxins we are almost as yet more in the dark than in our efforts to discover the exact nature of the poisons of germs. However, it has been possible to separate in a fairly pure form the antitoxic principle from diphtheria serum, a minute amount of which will confer immunity and the antitoxic principle of swine plague, .002 g. of which has been found to cure animals weighing 1 pound, and even a solid antitoxic-like substance for tuberculosis has been obtained in an impure form. All these solid antitoxic principles resemble each other very closely in their chemical tests and methods of separation showing albuminoid reactions, but in their curative properties they are totally independent the one of the other. The diphtheria antitoxic serum does not cure tetanus; the swine plague serum does not cure the cholera.

In the case of the venom of serpents it has been found that repeated injections will make the serum of an animal antitoxic and curative against other venoms. The antitoxic serum produced by the cobra venom will protect animals and men against the bite of the rattlesnake as well as its own bite. It would seem from this that there is a very close relationship between the poisons of venomous snakes and that immunity to one also gives protection from the other. It appears very probable also that the poisons of germs belonging to the same genus will be closely allied and that an antitoxin for one will also be an antitoxin for the other. In fact, it has been demonstrated that the products of the bacillus coli communis will protect animals from the typhoid germ to which it is closely allied. The same effect will probably be found with many other diseases where the germs are related.

The difficulty of separating these antitoxins completely from the other constituents of the blood has made it impossible as yet to obtain positive information as to their true chemical character.

As to their action in producing immunity one theory is that they directly neutralize the poisons which the germs produce, but this does not seem to be substantiated by experiment.

Another theory proposed first by Sternberg, then by Metchinkoff, ascribes immunity to the action of the white blood corpuscles upon the bacteria, while the third theory, and the one which seems most tenable in view of actual results, is that the antitoxic principle partakes of the nature of an unorganized ferment like diastase, and that its action in the body, with the aid of the leucocytes, suffices to render innocuous the poisons of the particular germs.

There is little room for doubt that in the first instance the antitoxins are the result of cell activity upon the introduced poison. Just how the cell manages to convert the toxin into antitoxic ferment is not known, probably by absorption of the toxin and subsequent secretion of the antitoxin within the cell-wall. Every added dose of toxin finds not only the leucocytes but a ferment to aid in its decomposition, and so the change proceeds more rapidly and the immunity is increased. Exactly what the chemical alteration in this instance is, has not been explained, but that there is oxidation, and molecular rearrangement of the toxin seems to be probable.

Thus without taking into consideration the destruction of the causes of disease, viz., germs themselves, by means of such excellent disinfectants as formaldehyde, has the warfare against the microbes progressed. Although as we learn more of the properties and uses of their toxins we are almost forced to confess that it is not a warfare, but rather that man is learning how to train and control these microscopic forms of life as centuries before he learned how to control the animals and higher plants.

Our ideas of germs are so thoroughly associated with disease that we often forget that these germs are but the simplest forms of plant cells which are endowed with various functions. The majority of them are not injurious to man, but very useful fellow-workers if he has once learned how to manage them. The value of this cell life in the production of wines, beer and other fermented liquids is too well known to need more than passing mention. But you may not all know to what extent the aroma and flavor of butter and cheese are due to the products of micro-organisms. Now these products are frequently ethers and esters, sometimes acid and acid derivatives or amines, the latter a class of compounds to one of which smoked herring owes its particular flavor and which is also formed by a number of bacteria.

When milk is first collected from healthy animals it is almost free from germs, but exposed to the air it soon becomes filled with those forms of life which are perfectly harmless. If placed under suitable conditions with regard to temperature they will multiply very readily and the milk becomes sour, due to the formation of lactic acid produced from the sugar in the milk by one or more of these germs. If the germs present happen to be those giving an ether and ester which have a pleasant flavor and aroma, good butter can be made, but if they give rise to the formation of disagreeable thio, ethers and esters or some amines, the butter is poor and bad

Now, by isolating different germs found in the milk and cultivating them separately, so as to discover their own peculiar product, it is possible to always make butter of the same sort and flavor by first destroying the other germs present by Pasteurization and then inoculating the cream with the particular germs desired. A number of germs have been isolated from milk which will produce good butter, and any one of them is, perhaps, as satisfactory as the other, the etheral product being slightly different and more palatable to different individuals. Of course, a great many germs have been found in milk which produce disagreeable compounds and it is not possible to tell from their appearance simply, which will be desirable plants, but it is easy to cultivate them in a small quantity of milk, note the results and select the desirable plant cells.

Fortunately or unfortunately the use of these germs has been patented, so that in the near future we may see branded upon particularly fine butter and cheese patented in 1893, amended 1896, reissued 1908, etc. May we expect soon a patented process for sterilized breathing, eating and sleeping?

Recently it has been found that malt if inoculated with a particular ferment from the skin of the grape will be converted into wine, the ferment used giving rise to the formation of characteristic ethers, so it is certainly not beyond the limits of possibilities that in the near future American beer after a voyage to France may return as excellent champagne. When we discover too a germ (as had been done recently) that converts starch into cellulose, we are almost led to wonder if it might not be possible to produce cotton in a culture flask if the particular germs were supplied with nutritious food and a sufficient amount of carbon dioxide, oxygen and water.

The flavor of many lucious fruits and foods is due to the products either directly or indirectly of one or more of these useful bacteria, and on the other hand similar germs play an important and as yet unknown rôle in the formation of poisonous alkaloids.

Many bacteria form beautifully colored substances, reds, yellows, blues, greens and delicate shades which the art of man has not been able to imitate and the nature of which he has not yet learned. These, too, are only hiding their secrets with a thin veil which investigation will soon withdraw.

But it is not only in simple industrial processes that the products of germs are important. Man's very existence, while menaced on the one hand by a few germs, is on the other dependent upon their activity. The germs which in the soil produce nitrous and nitric acid and ammonia, and aid their assimilation by the plants, those which facilitate the decomposition of phosphates and bring the phosphorous, a so necessary constituent for the life of plants and animals into an available form, and those which aid in the destruction of dead vegetable and animal matter, play a very valuable and but little appreciated part in the continuance of the life and well-being of man.

There are many other ways in which the products of these dreaded microscopic cells are useful, but all, a very insignificant number of which we have mentioned, are only waiting man's bidding to become valuable subjects, and to show that, as has been instanced in the history of nations, conquered people often make the best and wisest citizens.

E. A. DE SCHWEINITZ.

WASHINGTON, D. C.

THE GROWTH OF CHILDREN.

IN the years 1891 and 1892 I collected statistics on the growth of children in Worcester, Mass., mainly with a view to investigating individual growth. Although it was not possible, as was my original intention, to continue the series through a number of years, some results of interest have been obtained. The measurements were taken partly by myself, partly by fellows and students of Clark University. I am indebted to Dr. G. M. West for many of the measurements.

The stature of the same children was measured in May, 1891, and in May, 1892. The average annual increases and the variability of the amount of growth (the mean of the squares of individual variations) for these intervals were as follows:

AVERAGE INCREASES IN STATURE OF CHILDREN BETWEEN THE FOLLOWING YEARS (*cm.*).

	5 and 6	6 and 7	7 and 8	8 and 9	9 and 10	10 and 11	11 and 12	12 and 13	13 and 14	14 and 15	15 and 16
Boys	6.55	5.70	5.37	4.89	5.10	5.02	4.99	5.91	7.88	6.23	5.64
Girls	5.75	5.90	5.70	5.50	5.97	6.17	6.98	6.71	5.44	3.34	——

VARIABILITY OF ANNUAL GROWTH.

Boys	——	±0.68	±0.86	±0.96	±1.03	±0.88	±1.26	±1.86	±2.39	±2.91	±3.46
Girls	±0.88	±0.98	±1.10	±0.97	±1.23	±1.85	±1.89	±2.06	±2.89	±2.71	——